MSUK'S RESPONSE TO NICE CONSULTATION ON HST ROUTING CRITERIA

MSUK would like to thank NICE for the opportunity to feedback on the proposed HST changes through this consultation. Please find our response to the specific questions of the consultation below.

Do you have any comments related to routing criterion 1?

Routing criterion 1: The disease is ultra-rare and debilitating, that is, it:

- *is defined as having a point prevalence of 1:50,000 or less in England*
- *is lifelong after diagnosis with current treatment, and*
- *has an exceptional negative impact and burden on people with the disease*

- Many (ultra-)rare diseases do not have their own ICD-10 or ICD-11 code, but rather are part of a group code. For example, molybdenum cofactor deficiency type A is part of the ICD-10 group code E61.5 Molybdenum Deficiency, encompassing all different types of the disorder. Similarly, it is part of the ICD-11 group code 5B5K.A Molybdenum Deficiency, again encompassing all different types of the disorder. By utilising this narrow approach of ICD codes to determine what a disease is, the reality of (ultra-)rare diseases and their relatively undiscovered/unestablished status is ignored and a non-rare-disease-mentality is applied to rare diseases. Classifying by disease based on ICD codes would thereby also unjustly increase prevalence numbers.
    - An alternative that can be considered to ensure a specific disorder and not group of disorders is identified, is by making use of Orphacodes.

- It is unclear how "exceptional negative impact" will be judged: one person's value judgement does not equal another. More clarity is required.
    - Additionally, this criterion does not account for the fact that many rare diseases have multiple comorbidities. Many people will be using on- or off-label treatment to address this aspect of their rare disease. The "exceptional negative impact" requirement may end up excluding opportunities for new treatments for the treatment of the rare disorder itself, to be routed through HST.

Do you have any comments related to routing criterion 2?

Routing criterion 2: The technology is an innovation for the ultra-rare disease

- The requirement "not being explored in other indications" is unjust and inequitable for the rare disease community. When a treatment is being explored in other indications, there is no guarantee for a positive outcome; thereby this requirement limits the potential of a medicine which can have direct impact for the indication it is currently being considered for, considering that the clinical trials have proven a level of positive impact. It may also stifle innovation, research and development into other indications as a strategic consideration.

- It is unclear why repurposing should not be allowed. Repurposing is becoming increasingly popular and beneficial in (ultra-)rare diseases; not allowing this will limit the amount of companies pursuing repurposing options, thereby stifling research and development, and thus innovation, for (ultra-)rare diseases.
    - If there is to be a blanket exclusion of repurposing, NICE, together with NHS England, needs to put an alternative program in place to ensure incentives to pursue these options remain. Currently, such a program does not exist. Implementing this exclusion without a proper alternative will stifle research and development.

Do you have any comments related to routing criterion 3?

Routing criterion 3: No more than 300 people in England are eligible for the technology for its licensed indication, and the technology is not an individualised medicine.

- Within the HST criteria, two different prevalence measures are applied to the same population, with this second one substantially narrowing the eligible population. In criterion 1, an eligible population of approximately 1140 people in England is used (calculated from the prevalence value and English population numbers as of 2022 published by ONS). In this criterion, criterion 3, this original population of approximately 1140 is reduced to 300; an almost 75% reduction. Harmonisation of these values, as opposed to increasing the variation, considering an upper limit of 500 was previously considered, would be preferred and would increase clarity. In line with this, we disagree with the narrowing of the scope from 500 to 300 people.

- The requirement that a technology "has to be the first treatment for the 'licensed indication' under consideration" ignores the fact that not all technologies which have been either approved in the past, or historically been prescribed, make a real positive impact on the lives of people with a rare disease. The requirement to be "the first", stifles innovation, and suggests that if a treatment is available, that is good enough for people; thereby failing to acknowledge that more can be achieved for people with a rare disease. The definitions suggest a mindset of it being "good enough" for people to have a treatment available, rather than ensuring they get "the best" option.
    - This approach is inequitable in comparison to incentives that have been created for other, non-rare diseases, such as cancers, where the developers of incremental innovations are rewarded and people living with a cancer have a wider choice of treatment options.
    - Additionally, this approach suggests a lack of understanding of the rare disease market, where "me-too" products rarely ever happen; while simultaneously creating a barrier for rare disease research, development and innovation. In the handful of cases where something like this may occur, it would be more appropriate for NICE to assess them on a case-by-case basis rather than creating a pre-defined upfront barrier that stifles innovation.
    - Thus, this requirement creates an unfair and imbalanced landscape to people living with a rare disease in comparison to those with a non-rare disease.

Do you have any comments related to routing criterion 4?

Routing criterion 4: The technology is likely to offer substantial additional benefit for people over existing established clinical management, and the existing established clinical management is considered inadequate.

- Similar to criterion 1, it is unclear how "the existing established clinical management is considered inadequate" will be assessed; for example, a clinician might say that the clinical management is adequate, while the person living with the disorder says it is inadequate; or vice-versa. Whose value judgement on "inadequate clinical management" will be used and how will it be ensured that this is fair across treatments, but also for the people living with those disorders.

- The definition “there is no disease modifying treatment available in the NHS in England and Wales” ignores the multiple comorbidities common to many rare diseases. There should be no barrier to other disease modifying treatments being developed for people with a rare disease as they may address another substantial comorbidity. By removing incentives, the continued innovation, research and development in rare diseases will be stifled, especially in the absence of another incentive in the larger NHS framework.

Do you have any comments on the overall proposal for the refinement of the existing HST routing decision criteria?

While an attempt has been made to introduce more rigour in the highly specialised technology criteria, much ambiguity is still present with many of the criteria open to interpretation. With no clear guidance on how these criteria will be applied practically, the update creates no tangible benefit to the rare disease community.

Instead, numerous of the suggested amendments demonstrate a lack of understanding of the rare disease landscape, e.g. the requirement of ICD codes to define disorders, the instant dismissal of repurposed medicines and the requirement to be “the first treatment”. Through this, the new criteria fail to acknowledge the numerous hurdles the rare disease community already face and limits their chances of treatment innovation.

Finally, it should be acknowledged that these revised criteria will have an implication on the UK’s standing in international clinical trial research and market access roll out of new medicines. The criteria downgrade the UK market, which will have a measurable impact on people living with a rare disorder, receiving delayed or no access to transformative treatments which suggests and demonstrates that the rare disease population is not as important as the non-rare disease population.